

Applicant : Leonard Guarente et al.
Serial No. : 09/735,786
Filed : December 13, 2000
Page : 4

Attorney's Docket No.: 13407-016002 / MIT-8503

REMARKS

Applicants hereby submit that the enclosures fulfill the requirements under 37 C.F.R. §1.821-1.825. The amendments merely insert sequence identifiers in the specification and replace the original Sequence Listing with an amended substitute Sequence Listing. The substitute Sequence Listing contains the amino acid sequences "TLGL" and "FGGG" disclosed at page 63 of the specification, and "GAG(V/I)S(T/V)S (L/C/A)GIPDFRS" disclosed at page 42 of the specification, now SEQ ID NOs:36-38, respectively. No new matter has been added.

Further, applicants submit that the specification fulfills the requirements under 37 CFR § 1.821(d). In accordance with the rules, sequence identifiers for the sequences disclosed in Figures 2A, 2C, 5A, 6A, 12A, 14A, 19, 21A-21D, and 22 are positioned in the section entitled "Brief Description of the Figures" beginning at page 11 of the specification (MPEP § 2422.02). Applicants understand that no further amendments are required.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 13407-016002.

Respectfully submitted,

Date: 29 October

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"Version With Markings to Show Changes Made"

In the specification:

Paragraph beginning at page 42, line 19, has been amended as follows:

The term "core domain" (also referred to herein as "core") refers to the evolutionarily conserved domains [fo] of Sir2 or Sir2-like proteins which can be identified, for example, by the comparison of amino acid sequences by, for example, CLUSTAL X, BLAST, PSI-BLAST or FASTA algorithms. The "core domain" is the domain that shows significant identity and/or homology to about 240-270 amino acids of Sir2 or Sir2-like proteins (about 20-50% or higher as amino acid identity, see Figure 2) and/or possesses the consensus sequence GAG(V/I)S(T/V)S(L/C/A)GIPDFRS (SEQ ID NO:[27] 38) and YTNQID (SEQ ID NO: 28) (Brachmann, *et al.*, *Genes & Development* 9:2888-2902, (1995)). The "core domain" of Sir2 proteins has NAD-dependent deacetylation and/or mono-ADP-ribosylation activities. Any protein with a "core domain" of a Sir2 protein, a fragment of the core domain, or any functional or structural equivalent which is capable of NAD-dependent deacetylation and/or mono-ADP-ribosylation of nuclear proteins is within the scope of the invention.

Paragraph beginning at page 66, line 25, has been amended as follows:

TBLASTN searches were performed on the NCBI mouse EST sequence databases, using the amino acid sequence of ySir2p. All mouse EST sequences homologous to ySir2p were classified into three groups termed α , β , and γ , based on the homology results from the searches. Three representative EST cDNA clones were purchased for three mouse homolog groups from Genome Systems Inc (St. Louis, MO): AA199012 for α , AA105536 for β , and AA260334 for γ . The cDNA clones were partially or completely sequenced. All deduced amino acid sequences were aligned with the Clustal X program. To cover each core domain completely, amino acid sequences of AA137380 and AA212772 for β and γ respectively, were also used. A phylogenetic tree of the core domains of the yeast and mouse *Sir2* families was generated with the Clustal X and NJPLOT program by using the following amino acid sequences: position 228-499 for ySir2p, 174-440 for yHst1p, 1-251 for yHst2p, 26-315 for yHst3p, 65-343 for yHst4,

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Page : 6

215-460 for mSir2 α , TLGL (SEQ ID NO:36) to LINKEK (SEQ ID NO: 32) for mSir2 β , and
FGGG (SEQ ID NO:37) to LINRDL (SEQ ID NO: 33) for mSIR2 γ .